REMARKS

Claims 1-71 are pending in the application, claims 1 and 67-69 have been amended, and claims 4, 6-37, 44-66, 70 and 71 are withdrawn from consideration. Support for the claim amendments and additions may be found throughout the specification, including the claims as originally filed. No new matter has been added. In particular support for the amendments to the claims may be found, for example, at page 4, lines 9-15, page 4 line 30 to page 5, line 9, page 7, lines 30-31, page 10, lines 25-27, page 20, lines 16-18, etc.

Amendment of claims should in no way be construed as an acquiescence to any of the Examiner's rejections. The amendments to the claims are being made solely to expedite prosecution of the present application and do not, and are not intended to, narrow the claims in any way. Applicants reserve the option to further prosecute the same or similar claims in the instant or in a subsequent patent application.

Rejection of claims 1-3, 5, 38-43, 58-64, and 67-71 under 35 U.S.C. §112, second paragraph

Claims 1-3, 5, 38-43, 58-64, and 67-71 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. Applicants note that claims 2, 3, 5, 38-43 and 67-69 are dependent on claim 1 and therefore the arguments made below with respect to claim 1 are also applicable to the dependent claims. Claims 70 and 71 are withdrawn from consideration and therefore are not addressed. The rejection is respectfully traversed.

The Office Action alleges that "claim 1 already assumes that, for a given protein, [the] properties of a protein are already provided in a database." Applicants respectfully disagree with the rejection, however, in an effort to expedite prosecution of the application, claim 1 has been amended and the amendment is believed to obviate the rejection. In particular, applicants have amended the claim to clarify that the method relates, at least in part, to determination of at least one *unknown* biochemical or biophysical property of a protein. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

The Office Action further alleges that claim 1 is indefinite for recitation of the term "one or more" parameters. Applicants respectfully disagree with the rejection, however, in an effort to expedite prosecution of the application, claim 1 has been amended and the amendment is

believed to obviate the rejection. In particular, applicants have amended the claim to clarify that the method relates, at least in part, to correlating protein sequence information with biochemical and/or biophysical properties. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

The Office Action further alleges that claim 1 is indefinite for recitation of the term "analyzing" with reference to the sequence of a protein. Applicants respectfully disagree with the rejection, however, in an effort to expedite prosecution of the application, claim 1 has been amended and the amendment is believed to obviate the rejection. In particular, applicants have amended the claim to clarify that the database correlations are applied to the sequence of a target protein. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

The Office Action further alleges that claim 1 is indefinite for recitation of the term "correlating." Applicants respectfully disagree with the rejection, however, in an effort to expedite prosecution of the application, claim 1 has been amended and the amendment is believed to obviate the rejection. In particular, applicants have amended the claim to clarify that a data-mining technique is used to produce correlations between protein sequence and the biochemical and/or biophysical properties of a protein. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

The Office Action further alleges that claim 1 is indefinite because "it is unclear whether the database includes one [or] many proteins" and that it is not clear "whether the protein sequence, and protein properties which are correlated with the sequence belong to the same or different proteins." Applicants respectfully disagree with the rejection, however, in an effort to expedite prosecution of the application, claim 1 has been amended and the amendment is believed to obviate the rejection. In particular, applicants have amended the claim to clarify that the claims relate, at least in part, to correlations between the sequence and properties for the same protein. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Accordingly, Applicants submit that the claims as written would be understood by one of ordinary skill in the art in light of the specification. Therefore, reconsideration and withdrawal of the rejection of claims under 35 U.S.C. §112, second paragraph, is respectfully requested.

Rejection of claims 1-3, 5, 68 and 69 under 35 U.S.C. §102(b)

Claims 1-3, 5, 68 and 69 were rejected under 35 U.S.C. §102(b) as being anticipated by Payne et al. for reasons of record. Furthermore, the Office Action alleges that Payne et al. "describes [a] protein database wherein each yeast protein has an entry for protein sequence as well [as] for its properties" and that "one possible reading of the claim language [of the instant invention] is that it is drawn to determination of already known protein propert[ies]" (internal quotations omitted). The rejection is respectfully traversed.

As stated in the response filed on April 3, 2003, Payne et al. merely discloses an archive of yeast protein information from which users may retrieve a record. The database disclosed in Payne et al. contains information relating to proteins and *previously determined* properties for those proteins. In contrast, the presently claimed embodiment is directed, at least in part, to *determination of an unknown property* of a protein using correlations developed through analyzing a database with data-mining techniques. Payne et al. clearly does not teach a method for determining an unknown property of a protein and therefore does not anticipate the instantly claimed embodiment.

A claim is anticipated only if each and every element of the claim is found in a single prior art reference. The Payne et al. reference does not teach each and every element of the claims in the present application. Therefore, reconsideration and withdrawal of the rejection of claims under 35 U.S.C. 102(b) is respectfully requested.

Rejection of claims 1-3, 5, 68 and 69 under 35 U.S.C. §102(b)

Claims 1-3, 5, 68 and 69 were rejected under 35 U.S.C. §102(b) as being anticipated by Celis et al. The Office Action states that similar to Payne et al., "Celis et al teaches [a] protein database wherein each protein has an entry for protein sequence as well [as] for its properties." The rejection is respectfully traversed.

Like the Payne et al. reference, Celis et al. merely discloses an archive of protein information from which users may retrieve a record. The database disclosed in Celis et al. contains information relating to proteins and *previously determined* properties for those proteins. In contrast, the presently claimed embodiment is directed, at least in part, to *determination of an unknown property* of a protein using correlations developed through analyzing a database with

data-mining techniques. Celis et al. clearly does not teach a method for determining an unknown property of a protein and therefore does not anticipate the instantly claimed embodiment.

A claim is anticipated only if each and every element of the claim is found in a single prior art reference. The Celis et al. reference does not teach each and every element of the claims in the present application. Therefore, reconsideration and withdrawal of the rejection of claims under 35 U.S.C. 102(b) is respectfully requested.

Rejection of claims 1-3, 5, 68 and 69 under 35 U.S.C. §103(a)

Claims 1-3, 5, 68 and 69 were rejected under 35 U.S.C. §103(a) as being obvious over Payne et al. or Celis et al. The Office Action states that "the referenced database allows [one] to do search (data mine) using as an entry either protein sequence or protein properties" and therefore "it would be obvious to one skilled in the art that the database allows [one] to correlate protein sequence with protein characteristics." The rejection is respectfully traversed.

Obviousness can only be established by combining or modifying the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found explicitly or implicitly in the references themselves or in the knowledge generally available to one or ordinary skill in the art (see MPEP 2143.01). Furthermore, the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination (see MPEP 2143.01 citing *In re Mills*, 916 F.2d 680 (Fed. Cir. 1990)). Applicants respectfully assert that the Examiner has failed to provide a motivation to modify the disclosure of Payne et al. or Celis et al.

As discussed above, both Payne et al. and Celis et al. merely describe databases containing information relating to protein sequence and other previously determined properties of proteins. For example, Payne et al. describes the Yeast Protein Database (YPD) which contains information relating to proteins of the budding yeast, *Saccharomyces cerevisiae*. For each protein contained in the database, there is a *report* which may contain information about properties of that protein such as, for example, molecular weight, isoelectric point, subcellular localization, and post-translational modifications. Users may *retrieve previously determined information* from the database by searching for a keyword, by protein name or by a protein property category. However, Payne et al. does *not* teach or suggest the *determination of an*

unknown property of a protein using data mining techniques to analyze a database thereby producing correlations which may be applied to a protein sequence of interest to determine the unknown property. Furthermore, Payne et al. describe their efforts as "curatorial" (see e.g., page 62 of Payne et al., left column). Therefore, Payne et al. merely describes the recordation of information and would not motivate one of skill in the art to manipulate a data set in order to determine unknown protein properties.

Similar to Payne et al., Celis et al. also describes a database which allows users to *retrieve previously determined information*. In particular, Celis et al. describes the current status of human and mouse proteomic 2D PAGE databases which may be used to study global gene expression both in health and disease (see e.g., Celis et al. page 65, left column, second paragraph). For example, the Keratinocyte 2D PAGE database contains images of 2D PAGE gels which allows a user to retrieve information on a protein by clicking on a spot in the gel image that corresponds to the protein of interest. The information relating to the proteins has been previously experimentally determined (see e.g., Celis et al. page 65, right column). However, Celis et al. does ***not*** teach or suggest the *determination of an unknown property* of a protein using data mining techniques to analyze a database thereby producing correlations which may be applied to a protein sequence of interest to determine the unknown property. Therefore, Celis et al. merely describes the recordation of information and would not motivate one of skill in the art to manipulate a data set in order to determine unknown protein properties.

Applicants respectfully remind the Examiner that the references must be viewed as a whole and must suggest the desirability of the claimed invention without the benefit of impermissible hindsight reconstruction afforded by the claimed invention. Furthermore, in order "[t]o establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." MPEP §2143.03 citing *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Neither Payne et al. nor Celis et al., either alone or in combination, teach or suggest each and every element of the embodiment presently claimed. Accordingly, the cited references, either alone or in combination, fail to teach or suggest the currently claimed embodiments. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of claims 1-3, 5, 68 and 69 under 35 U.S.C. §102(b)

Claims 1-3, 5, 68 and 69 were rejected under 35 U.S.C. §102(b) as being anticipated by Kim et al. The Office Action alleges that Kim et al. "teach [a] method of identification of novel proteins from databases by data mining using physico-chemical properties of proteins" and that "a database is searched using amino-acid property index, such as solubility, sequences of interest are identified and correlated with the physico-chemical property." The rejection is respectfully traversed.

Applicants wish to point out to the Examiner that Kim et al. is not a proper reference under 35 U.S.C. §102(b) because the reference was *not* published more than one year prior to the date of filing of the instant application.

Kim et al. is directed to a new algorithm for *identifying* multi-transmembrane *proteins* such as G Protein-Coupled Receptors (GPCR) from large-scale genomic databases (see e.g., Kim et al. page 767, right column, first paragraph). Kim et al. does *not* teach or suggest the *determination of an unknown property* of a protein using data mining techniques to analyze a database thereby producing correlations which may be applied to a protein sequence of interest to determine the unknown property.

Furthermore, Kim et al. appears to teach away from the currently claimed embodiment. In particular, contrary to the statements in the Office Action, Kim et al. ruled out solubility as a useful discriminating characteristic. Kim et al. discloses that seven different profiles (e.g., GES hydropathy index, Kyte-Doolittle index, polarity, pI, molecular weight, solubility, and alpha helix index) were characterized by two statistics (e.g., average periodicity and variance of 1st order derivative) to yield 14 variables that were first used for the discrimination (e.g., average periodicity of the GES, first derivative of the GES, average periodicity of polarity, first derivative of polarity, etc.). These variable were then subjected to a *step-wise deletion analysis* to "reduce the number of *spurious variables* which may result in *over-fitting the data*" (emphasis added) (see e.g., Kim et al., page 769, right column, and page 770, right column, third paragraph). After this deletion analysis four variables were settled on as useful for classification of GPCR and non-GPCR proteins: amino-acid usage index, log of the average periodicity of the GES scale, log of the average periodicity of the polarity scale, and variance of the first derivative of the polarity scale (*supra*). Accordingly, *solubility was eliminated* from Kim's analysis as a

"spurious variable" that may result in "over-fitting the data." Therefore, Kim et al. would teach away from the use of solubility in relation to developing correlations between a protein sequence and biochemical and/or biophysical properties thereof.

A claim is anticipated only if each and every element of the claim is found in a single prior art reference. The Kim et al. reference clearly does not teach each and every element of the claims in the present application. Therefore, reconsideration and withdrawal of the rejection of claims under 35 U.S.C. 102(b) is respectfully requested.

Rejection of claims 39-43 under 35 U.S.C. §103(a)

Claims 39-43 were rejected under 35 U.S.C. §103(a) as being obvious over Payne et al. or Celis et al. or King et al. The Office Action alleges that "[i]t would have been obvious to one skilled in the art to select an appropriate data mining method through routine experimentation." The rejection is respectfully traversed.

As discussed above, Payne et al. and Celis et al. fail to teach or suggest the *determination of an unknown property* of a protein using data mining techniques to analyze a database thereby producing correlations which may be applied to a protein sequence of interest to determine the unknown property. Payne et al. and Celis et al. merely disclose databases that may contain information such as protein sequence and previously determined protein characteristics. Therefore, these references merely describes the recordation of information and would not motivate one of skill in the art to manipulate a data set in order to determine unknown protein properties. Accordingly, there would be no motivation for one of skill in the art to use any well known data mining technique for the determination of an unknown protein property based on the teachings of either Payne et al. and/or Celis et al. Neither Payne et al. nor Celis et al., either alone or in combination, teach or suggest each and every element of the embodiment presently claimed. Accordingly, the cited references, either alone or in combination, fail to teach or suggest the currently claimed embodiments. Reconsideration and withdrawal of the rejection is respectfully requested.

Applicants note that the Office Action fails to make any statements about King et al. Should the Examiner wish to specifically address the King et al. reference applicants would be happy to further consider this reference. However, in the absence of any specific comments

regarding King et al., the Examiner has clearly failed to establish a *prima facie* case of obviousness. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Applicants believe that the remarks made herein fully address all issues raised in the Office Action. Silence with regard to any of the Examiner's rejections is not an acquiescence to such rejections. Specifically, silence with regard to Examiner's rejection of a dependent claim, when such claim depends from an independent claim that Applicant considers allowable for reasons provided herein, is not an acquiescence to such rejection of the dependent claim(s), but rather a recognition by Applicant that such previously lodged rejection is moot based on Applicant remarks and/or amendments relative to the independent claim (that Applicant considers allowable) from which the dependent claim(s) depends.
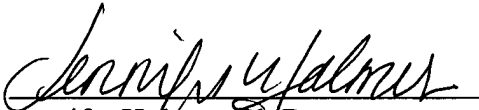
CONCLUSION

Applicants consider the Response herein to be fully responsive to the referenced Office Action. Based on the above Remarks, it is respectfully submitted that this application is in condition for allowance. Accordingly, allowance is requested. If a telephone conversation with Applicant's Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 832-1000.

Respectfully submitted,

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